REMARKS

The Examiner is respectfully requested to acknowledge applicants' claim for priority under 35 USC 119 and receipt of the certified copy of the priority document that was filed on August 9, 2001.

Claim 19 was rejected under 35 USC 112, second paragraph, for the reasons set forth at the middle of page 2 of the Office Action.

Claim 19 was amended to avoid the 35 USC 112, second paragraph rejection.

It is respectfully submitted that the present claims comply with all the requirements of 35 USC 112.

The other amendments to the claims involve only editorial revisions.

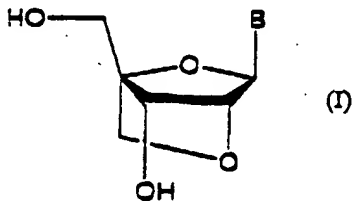
Claims 1 to 77 were rejected under 35 USC 103 as being unpatentable over WO 98/39352 to Imanishi et al. in combination with Obika et al., Tetrahedron Letters, 39, 5401-5404 (1998) for the reasons set forth on pages 3 and 4 of the Office Action.

It is admitted in the Office Action that both Imanishi et al. and Obika et al. do not teach the 2 carbon link between the

2'oxygen and the 4'carbon, as included in applicants' claimed compounds.

Submitted concomitantly herewith is a DECLARATION UNDER 37 CFR 1.132 of Dr. Makoto KOIZUMI, which provides a showing of unexpected results for the presently claimed invention.

The references cited in the Office Action contain a 2'-O,4'-O-methylene nucleoside having the following structure (I):



(I)

The enclosed KOIZUMI DECLARATION includes comparison test results for the following compounds:

Oligonucleotide A which contains the 2'O,4'-C-methylene nucleoside and which was synthesized according to the method described in WO 98/39352.

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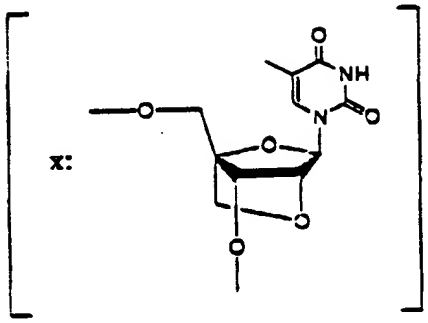
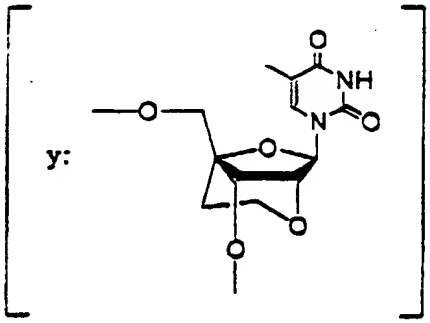
Oligonucleotide A: 5'-ttt ttt ttt txt-3'



Oligonucleotide B according to the presently claimed invention

Oligonucleotide B: 5'-ttt ttt ttt tyt-3'



The resistance of oligonucleotide A and oligonucleotide B was tested against snake venom phosphodiesterase according to the method of Test Example 2 of the present specification. The results are shown in Table 1 of the KOIZUMI DECLARATION, which is reproduced as follows:

A

Table 1. **Percentage of remaining oligonucleotides.**

Sample	0 min	30 min	120 min
Oligonucleotide A	100	15	not detected
Oligonucleotide B (according to the presently claimed invention)	100	90	82

The above results show that whereas oligonucleotide A was no longer detected after 120 minutes of incubation, 82% of oligonucleotide B according to the presently claimed invention still remained. Oligonucleotide B of the presently claimed invention has an unexpectedly much higher nuclease resistance activity than oligonucleotide A. It is respectfully submitted that the remarkably high nuclease resistance activity of the compound of the presently claimed invention would not be obvious to a person of ordinary skill in the art.

It is therefore respectfully submitted that applicants' claimed invention is not rendered obvious over the references, either singly or combined in the manner relied upon in the Office Action, in view of the distinctions discussed hereinabove. It is furthermore submitted that there are no teachings in the

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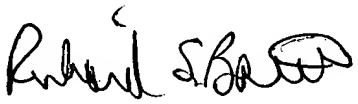
references to combine them in the manner relied upon in the Office Action.

Reconsideration is requested. Allowance is solicited.

If the Examiner has any comments, questions, objections or recommendations, the Examiner is invited to telephone the undersigned at the telephone number given below for prompt action.

Respectfully submitted,



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Enc.: DECLARATION UNDER 37 CFR 1.132 of Dr. Makoto KOIZUMI dated September 2, 2003

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Serial No.	: 09/925,673
Applicants	: Masakatsu KANEKO et al.
Filed	: August 9, 2001
For	: NOVEL NUCLEOSIDE AND OLIGONUCLEOTIDE ANALOGUES
Art Unit	: 1623
Examiner	: Howard Owens, Jr.
Docket No.	: 01376CIP/HG
Customer No.	: 01933
Confirmation No.	: 4630

DECLARATION UNDER 37 CFR 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

S I R :

I, Dr. Makoto KOIZUMI, declare as follows:

1. I graduated from the University of Hokkaido Univ. in the year 1991, and I received the degree of Ph. D.

2. I have worked for Sankyo Co., Ltd., Tokyo, Japan, in the Exploratory Chemistry Research Laboratories since 1991, and I presently hold the position of Associate Chief Researcher.

3. The following experiments were carried out under my supervision.

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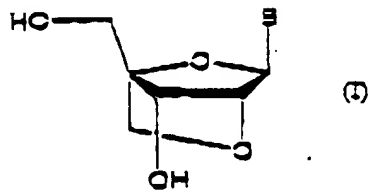
Compounds of the above-identified patent application were evaluated for nuclease resistance. From the results, it is clear that the compounds of the present invention patentably distinguish over the prior art cited in the July 29, 2003 Office Action.

Methods and Results

(a) Synthesis of a reference compound

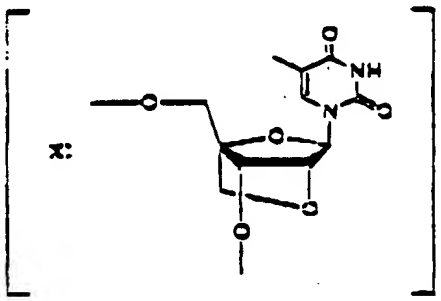
The references cited by the Examiner in the July 29, 2003 Office Action contain a 2'-O,4'-C-methylene nucleoside having the following structure (I):



(I)

Oligonucleotide A, which contains the 2'-O,4'-C-methylene nucleoside of (I), was synthesized according to the method described in WO 98/39352 and its nuclease resistance was compared with an oligonucleotide containing the presently claimed nucleoside.

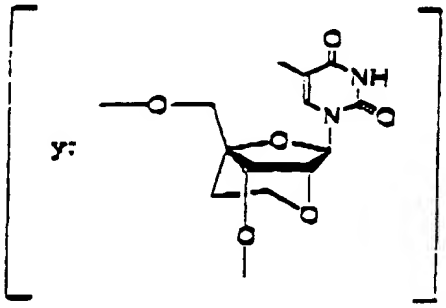
Oligonucleotide A: 5'-tx tx tx tx-3'



(b) Synthesis of a compound of the above-identified patent application

Oligonucleotide B, which contains the presently claimed nucleoside, was synthesized according to the method described in the specification of the above-identified application.

Oligonucleotide B: 5'-m nt mt tyt-3'



(c) Assay method of nuclease resistance of oligonucleotides and results

The resistance of oligonucleotide A and oligonucleotide B were tested against snake venom phosphodiesterase according to the method of Test Example 2 on page 107 of the above-identified patent application. The oligonucleotides in an amount of 26 μg/ml were added to a solution containing 50 mM Tris·HCl (pH 8.0) and 10 mM $MgCl_2$. The nuclease resistance activity is defined as the percent ratio of remaining oligonucleotides compared with the initial levels. The results are shown in the following Table 1.

Table 1. Percentage of remaining oligonucleotides.

Sample	0 min	30 min	120 min
Oligonucleotide A	100	15	not detected
Oligonucleotide B (according to the presently claimed invention)	100	90	32

As seen from the above Table 1, whereas oligonucleotide A was no longer detected after 120 minutes of incubation, 82% of oligonucleotide B according to the presently claimed invention still remained. Oligonucleotide B of the presently claimed invention had an unexpectedly much higher nuclease resistance activity than oligonucleotide A. The remarkably high nuclease resitance activity of a compound of the presently claimed invention is unexpected and would not be obvious to a person of ordinary skill in the art. Since the role of the ring structure of the presently claimed invention is not only structural, the compounds according to the presently claimed invention are considered to patentably distinguish over the cited prior art.

I hereby declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001, of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: Sep. 12 2003 By: Makoto Koizumi

Makoto KOIZUMI, Ph. D.